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Jeff Steven Grotelucschen Hall

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EXAMINER

SITTON, JEHANNE SOUAYA

ART UNIT

PAPER NUMBER

1634

DATE MAILED: 05/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| | | | |
|------------------------------|------------------------|---------------------------|--|
| Office Action Summary | Application No. | Applicant(s) | |
| | 10/074,328 | GROTELUESCHEN HALL ET AL. | |
| | Examiner | Art Unit | |
| | Jehanne S. Sitton | 1634 | |

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 March 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 101, 104-106 and 111-125 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 101, 104-106, and 111-125 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. Currently, claims 101, 104-106 and 111-125 are pending in the instant office action. All the amendments and arguments have been thoroughly reviewed but are deemed insufficient to place this application in condition for allowance. The following rejections are reiterated. They constitute the complete set being presently applied to the instant Application. Response to Applicant's arguments follow. This action is FINAL.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. The rejection under 35 USC 112/2nd paragraph is withdrawn in view applicant's arguments made at page 7 of the response.

4. The terminal disclaimer filed 3/13/2006 has been approved. Accordingly, the rejections made under Obviousness type double patenting at sections 18-21 of the previous office action have been withdrawn.

Maintained Rejections

Claim Rejections - 35 USC § 102

5. Claims 101, 104, 111-117, and 123-125 rejected under 35 U.S.C. 102(b) as being anticipated by Harrington (Harrington et al.; The EMBO Journal, vol 13, pp 1235-1246, 1994).

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With regard to claim 101, Harrington teaches a set of oligonucleotides as follows: 1) a target nucleic acid HJ41 (Figure 8a, lanes 3-5) (claims 114-115, it is noted that the claims do not require that the first and second target be different, therefore more than one copy of the target nucleic acid can be considered first, second, third, etc, target nucleic acids. Alternatively, any of the other nucleic acids taught by Harrington - see page 1245, col 1 "oligonucleotides" - can be considered a second "target" nucleic acid, as claim 115 does not provide any structural limitations with regard to the "second target nucleic acid"), 2) a first oligonucleotide HJ40 comprising a charged adduct and a portion completely complementary to the target (a "charged adduct" is broadly interpreted to encompass a single nucleotide or charged phosphate group; with regard to claim 125, HJ40 comprises an uncleavable region) alternatively, HJ42 can be considered a first oligonucleotide as it comprises a portion completely complementary a first region of a target nucleic acid; 3) a second oligonucleotide HJ39, comprising a 3' portion and a 5' portion completely complementary to a second region of the target nucleic acid downstream of and contiguous to said first region; and 4) FEN-1, a thermostable 5' nuclease lacking synthetic activity which comprises an amino acid sequence wherein a portion is homologous to a portion of an amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism (claim 111). It is noted that the term thermostable has been broadly interpreted to encompass a nuclease which is stable at a specific temperature. The specification does not define the term to be limited to stability at any particular temperature. With regard to claim 104, Harrington teaches administering such oligonucleotides to a gel, which is considered a solid support. With regard to claim 112, Harrington teaches a buffer solution (see page 1245). With regard to claim 113, Harrington teaches a third oligonucleotide HJ49, complementary to a third

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region of said target nucleic acid upstream of said first region of said target nucleic acid. It is noted that the term “providing” in claim 113 has been given no weight as the claims are drawn to products and not to methods requiring a step such as “providing”. With regard to claim 116, the claim sets forth no structural limitations for “linker”. Therefore the term has been given it’s broadest reasonable meaning which encompasses the sugar group of the nucleotide. With regard to claim 117, any nucleotide or nucleic acid is detectable. Alternatively, molecule HJ42 comprises a label at it’s 5’ end (claim 123). With regard to claim 124, either HJ42 or HJ40 comprise an uncleavable region.

6. Claims 101, 104, 111-117, and 123-125 are rejected under 35 U.S.C. 102(b) as being anticipated by Harrington II (Harrington et al; Journal of Biological Chemistry, vol. 270, pp 4503-4508, 1995).

With regard to claim 101, Harrington II teaches a set of oligonucleotides as follows: 1) a target nucleic acid AI4 (Figure 5a, lanes 11-14; 5b, lanes 11-15) (claims 114-115, it is noted that the claims do not require that the first and second target be different, therefore more than one copy of the target nucleic acid can be considered first, second, third, etc, target nucleic acids. Alternatively, any of the other nucleic acids taught by Harrington - see page 4503, col 2 “oligonucleotides”- can be considered a second “target” nucleic acid, as claim 115 does not provide any structural limitations with regard to the “second target nucleic acid”), 2) a first oligonucleotide HJ46 comprising a charged adduct and a portion completely complementary to the target (a “charged adduct” is broadly interpreted to encompass a single nucleotide or charged phosphate group; with regard to claim 125, HJ46 comprises an uncleavable region); 3) a second

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oligonucleotide HJ77, comprising a 3' portion and a 5' portion completely complementary to a second region of the target nucleic acid downstream of and contiguous to said first region; and 4) FEN-1, a thermostable 5' nuclease lacking synthetic activity which comprises an amino acid sequence wherein a portion is homologous to a portion of an amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism (claim 111). It is noted that the term thermostable has been broadly interpreted to encompass a nuclease which is stable at a specific temperature. The specification does not define the term to be limited to stability at any particular temperature. With regard to claim 104, Harrington II teaches administering such oligonucleotides to a gel, which is considered a solid support. With regard to claim 112, Harrington II teaches a buffer solution (see page 4504). With regard to claim 116, the claim sets forth no structural limitations for "linker". Therefore the term has been given it's broadest reasonable meaning which encompasses the sugar group of the nucleotide. With regard to claim 117, any nucleotide or nucleic acid is detectable. Alternatively, molecule HJ46 comprises a label at it's 5' end (claim 123). With regard to claim 124, HJ46 comprises an uncleavable region as it comprises regions not cleaved in the reaction.

Response to Arguments

7. The response traverses both rejection under 35 USC 102(b) over Harrington I, and in the alternative, Harrington II. The response asserts that neither Harrington I or II teach a thermostable 5' nucleic lacking synthetic activity, but rather teach a nuclease used at 30°C, not one that is functional or active at about 55°C or higher. This argument has been thoroughly reviewed but was found unpersuasive. In response to applicant's argument that the references

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fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). In the instant case, the claims do not limit the 5' nuclease as "functional or active at about 55°C or higher". As noted in the previous office action and reiterated above, the specification does not limit the term to stability at a particular temperature. The response asserts that this interpretation is incorrect because the specification teaches at page 32, lines 16-18, that enzymes that are "functional or active (ie: that can perform catalysis) at an elevated temperature, ie: at about 55°C or higher". This argument as well as the specification have been thoroughly reviewed but were not found persuasive to overcome the rejection because the specific temperature recitations provide examples of preferred limitations or embodiments. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). The response provides no reasoning as to why Harrington I or II do not teach the nucleic acid structures recited in the claims, other than stating so. However, Harrington I and II, as noted above, teach the remaining structures within the claims. For these reasons and the reasons already made of record, the rejections are maintained.

Claim Rejections - 35 USC § 103

8. Claims 105 and 106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrington in view of Dahlberg (WO 94/29482).

Harrington teaches a set of oligonucleotide structures that include nucleic acid sequences with unhybridized 3' termini or 5' termini and teaches analysis of cleavage of such structures using a 5' nuclease lacking synthetic activity. Harrington teaches among other reagents: 1) a target nucleic acid HJ41 (Figure 8a, lanes 3-5), 2) a first oligonucleotide HJ40 comprising a charged adduct and a portion completely complementary to the target (a "charged adduct" is broadly interpreted to encompass a single nucleotide or charged phosphate group) alternatively, HJ42 can be considered a first oligonucleotide as it comprises a portion completely complementary a first region of a target nucleic acid; 3) a second oligonucleotide HJ39, comprising a 3' portion and a 5' portion completely complementary to a second region of the target nucleic acid downstream of and contiguous to said first region; and 4) FEN-1, a thermostable 5' nuclease lacking synthetic activity which comprises an amino acid sequence wherein a portion is homologous to a portion of an amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism (claim 111). It is noted that the term thermostable has been broadly interpreted to encompass a nuclease which is stable at a specific temperature. The specification does not define the term to be limited to stability at any particular temperature. Harrington does not teach a method wherein the first oligonucleotide (claims 105) or the second oligonucleotide (claim 106) is attached to a solid support, however Dahlberg teaches a method wherein cleavage structures as taught by Harrington are subjected to cleavage reactions with 5' nucleases, as taught by Harrington wherein oligonucleotides of the cleavage structure are attached to solid supports (see pages 11-12, figure 23), whereby cleaves structures are released from the immobilized structure for further analysis. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to

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immobilize the first or second oligonucleotide taught by Harrington to a solid support as taught by Dahlberg. The ordinary artisan would have been motivated to attach either the first or second oligonucleotide in the cleavage structures of Harrington to a solid support as taught by Dahlberg for ease of cleavage detection as taught by Dahlberg.

9. Claims 105 and 106 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrington II in view of Dahlberg.

Harrington II teaches a set of oligonucleotide structures that include nucleic acid sequences with unhybridized 3' termini, 5' termini, or both, and teaches analysis of cleavage of such structures using a 5' nuclease lacking synthetic activity. Harrington II teaches among other reagents: 1) a target nucleic acid AI4 (Figure 5a, lanes 11-14; 5b, lanes 11-15), 2) a first oligonucleotide HJ46 comprising a charged adduct and a portion completely complementary to the target (a "charged adduct" is broadly interpreted to encompass a single nucleotide or charged phosphate group); 3) a second oligonucleotide HJ77, comprising a 3' portion and a 5' portion completely complementary to a second region of the target nucleic acid downstream of and contiguous to said first region; and 4) FEN-1, a thermostable 5' nuclease lacking synthetic activity which comprises an amino acid sequence wherein a portion is homologous to a portion of an amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism. It is noted that the term thermostable has been broadly interpreted to encompass a nuclease which is stable at a specific temperature. The specification does not define the term to be limited to stability at any particular temperature. Harrington II does not teach assays wherein the first oligonucleotide (claims 105) or the second oligonucleotide (claim 106) is attached to a

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solid support, however Dahlberg teaches a method wherein cleavage structures as taught by Harrington are subjected to cleavage reactions with 5' nucleases, as taught by Harrington II wherein oligonucleotides of the cleavage structure are attached to solid supports (see pages 11-12, figure 23), whereby cleavage structures are released from the immobilized structure for further analysis. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to immobilize the first or second oligonucleotide taught by Harrington II to a solid support as taught by Dahlberg. The ordinary artisan would have been motivated to attach either the first or second oligonucleotide in the cleavage structures of Harrington II to a solid support as taught by Dahlberg for ease of cleavage detection as taught by Dahlberg.

10. Claims 105-106, 118-119 and 122 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrington in view of Urdea.

Harrington teaches a set of oligonucleotide structures that include nucleic acid sequences with unhybridized 3' termini or 5' termini and teaches analysis of cleavage of such structures using a 5' nuclease lacking synthetic activity. Harrington teaches among other reagents, 1) a target nucleic acid HJ41 (Figure 8a, lanes 3-5), 2) a first oligonucleotide HJ40 comprising a charged adduct and a portion completely complementary to the target (a "charged adduct" is broadly interpreted to encompass a single nucleotide or charged phosphate group) alternatively, HJ42 can be considered a first oligonucleotide as it comprises a portion completely complementary a first region of a target nucleic acid; 3) a second oligonucleotide HJ39, comprising a 3' portion and a 5' portion completely complementary to a second region of the

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target nucleic acid downstream of and contiguous to said first region; and 4) FEN-1, a thermostable 5' nuclease lacking synthetic activity which comprises an amino acid sequence wherein a portion is homologous to a portion of an amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism (claim 111). It is noted that the term thermostable has been broadly interpreted to encompass a nuclease which is stable at a specific temperature. The specification does not define the term to be limited to stability at any particular temperature. Harrington does not teach a method wherein the first oligonucleotide (claim 105) or the second oligonucleotide (claim 106) is attached to a solid support or wherein the first oligonucleotide comprising a charged adduct comprises a detectable molecule which is fluorescein (claims 118-119) or wherein the charged adduct comprises at least one amino modified base (claim 122), however Urdea teaches detection of cleaved labeled nucleic acid molecules attaches to a solid support wherein separation of the label from the solid support is detected and indicates cleavage (col. 8, lines 47-55, Figures 2 and 3). Urdea further teaches labeling the nucleic acid with fluorescein which is incorporated on an amino modified base such as cytosine or uracil (col. 9, lines 45-50). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to label the first oligonucleotide of Harrington with fluorescein on an amino modified base, and to attach either the first oligonucleotide or the second oligonucleotide on a solid support as taught by Urdea because Urdea teaches detection of cleaved nucleic acids by separation of a labeled nucleic acid from a solid support and teaches labels such as fluorescein on an amino modified base can be used. The ordinary artisan would have been motivated to improve the method of Harrington

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with the use of the solid support and labeled nucleic acid as taught by Urdea for ease of detection as taught by Urdea and to minimize the use of radioactively labels.

11. Claims 105-106, 118-119, and 122 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrington II in view of Urdea.

Harrington II teaches a set of oligonucleotide structures that include nucleic acid sequences with unhybridized 3' termini, 5' termini, or both, and teaches analysis of cleavage of such structures using a 5' nuclease lacking synthetic activity. Harrington II teaches among other reagents: 1) a target nucleic acid AI4 (Figure 5a, lanes 11-14; 5b, lanes 11-15), 2) a first oligonucleotide HJ46 comprising a charged adduct and a portion completely complementary to the target (a "charged adduct" is broadly interpreted to encompass a single nucleotide or charged phosphate group); 3) a second oligonucleotide HJ77, comprising a 3' portion and a 5' portion completely complementary to a second region of the target nucleic acid downstream of and contiguous to said first region; and 4) FEN-1, a thermostable 5' nuclease lacking synthetic activity which comprises an amino acid sequence wherein a portion is homologous to a portion of an amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism. It is noted that the term thermostable has been broadly interpreted to encompass a nuclease which is stable at a specific temperature. The specification does not define the term to be limited to stability at any particular temperature. Harrington II does not teach a method wherein the first oligonucleotide (claims 105) or the second oligonucleotide (claim 106) is attached to a solid support or wherein the first oligonucleotide comprising a charged adduct comprises a detectable molecule which is flourescein (claims 118-119) or wherein the charged

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adduct comprises at least one amino modified base (claim 122), however Urdea teaches detection of cleaved labeled nucleic acid molecules attaches to a solid support wherein separation of the label from the solid support is detected and indicates cleavage (col. 8, lines 47-55, Figures 2 and 3). Urdea further teaches labeling the nucleic acid with fluorescein which is incorporated on an amino modified base such as cytosine or uracil (col. 9, lines 45-50). Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to label the first oligonucleotide of Harrington II with fluorescein on an amino modified base, and to attach either the first oligonucleotide or the second oligonucleotide on a solid support as taught by Urdea because Urdea teaches detection of cleaved nucleic acids by separation of a labeled nucleic acid from a solid support and teaches labels such as fluorescein on an amino modified base can be used. The ordinary artisan would have been motivated to improve the method of Harrington II with the use of the solid support and labeled nucleic acid as taught by Urdea for ease of detection as taught by Urdea and to minimize the use of radioactive labels.

12. Claims 120-121 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrington in view of Corey.

Harrington II teaches a set of oligonucleotide structures that include nucleic acid sequences with unhybridized 3' termini or 5' termini and teaches analysis of cleavage of such structures using a 5' nuclease lacking synthetic activity. Harrington teaches among other reagents: 1) a target nucleic acid AI4 (Figure 5a, lanes 11-14; 5b, lanes 11-15), 2) a first oligonucleotide HJ46 comprising a charged adduct and a portion completely complementary to the target (a "charged adduct" is broadly interpreted to encompass a single nucleotide or charged

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phosphate group); 3) a second oligonucleotide HJ77, comprising a 3' portion and a 5' portion completely complementary to a second region of the target nucleic acid downstream of and contiguous to said first region; and 4) FEN-1, a thermostable 5' nuclease lacking synthetic activity which comprises an amino acid sequence wherein a portion is homologous to a portion of an amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism. It is noted that the term thermostable has been broadly interpreted to encompass a nuclease which is stable at a specific temperature. The specification does not define the term to be limited to stability at any particular temperature. Harrington does not teach wherein the first oligonucleotide comprises a charged adduct which comprises at least one amino acid (claim 120), wherein the amino acid is lysine, arginine, aspartate, or glutamate (claim 121), however Corey teaches that the addition of positively charged peptides in a nucleic acid sequence accelerates and enhances hybridization of that nucleic acid sequence, and that peptides containing as few as four lysines increased K_a by 5 fold. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the assays of Harrington with the use of positively charged peptides taught by Corey in the oligonucleotide structures of Harrington, including the first oligonucleotide. The ordinary artisan would have been motivated to modify the oligonucleotides of Harrington for the purpose of accelerating hybridization, as taught by Corey, in the assays of Harrington, and thus enhancing the assays of Harrington.

13. Claims 120-121 are rejected under 35 U.S.C. 103(a) as being unpatentable over Harrington II in view of Corey.

Harrington II teaches a set of oligonucleotide structures that include nucleic acid sequences with unhybridized 3' termini, 5' termini, or both, and teaches analysis of cleavage of such structures using a 5' nuclease lacking synthetic activity. Harrington II teaches among other reagents: 1) a target nucleic acid AI4 (Figure 5a, lanes 11-14; 5b, lanes 11-15), 2) a first oligonucleotide HJ46 comprising a charged adduct and a portion completely complementary to the target (a "charged adduct" is broadly interpreted to encompass a single nucleotide or charged phosphate group); 3) a second oligonucleotide HJ77, comprising a 3' portion and a 5' portion completely complementary to a second region of the target nucleic acid downstream of and contiguous to said first region; and 4) FEN-1, a thermostable 5' nuclease lacking synthetic activity which comprises an amino acid sequence wherein a portion is homologous to a portion of an amino acid sequence of a thermostable DNA polymerase derived from a thermophilic organism. It is noted that the term thermostable has been broadly interpreted to encompass a nuclease which is stable at a specific temperature. The specification does not define the term to be limited to stability at any particular temperature. Harrington II does not teach wherein the first oligonucleotide comprises a charged adduct which comprises at least one amino acid (claim 120), wherein the amino acid is lysine, arginine, aspartate, or glutamate (claim 121), however Corey teaches that the addition of positively charged peptides in a nucleic acid sequence accelerates and enhances hybridization of that nucleic acid sequence, and that peptides containing as few as four lysines increased K_a by 5 fold. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to improve the assays of Harrington II with the use of positively charged peptides taught by Corey in the oligonucleotide structures of Harrington II, including the first oligonucleotide. The ordinary

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artisan would have been motivated to modify the oligonucleotides of Harrington II for the purpose of accelerating hybridization, as taught by Corey, in the assays of Harrington II, and thus enhancing the assays of Harrington II.

Response to Arguments

14. The response traverses all rejections under 35 USC 103, which utilize Harrington I or II as primary reference, under the same grounds. The response asserts that neither Harrington I or II teach the combination of “first and second oligonucleotides that comprise defined regions of complementarity to a target nucleic acid such that they form an overlapped structure when annealed to the target nucleic acid; and a [2] thermostable 5’ nuclease lacking synthetic activity” and that none of the secondary references of Dahlberg, Corey, or Urdea overcome these deficiencies. These arguments have been thoroughly reviewed but were found unpersuasive. As noted above, the response does not provide any specific reasoning as to why Harrington I or II do not teach the nucleic acid structures in claim 101. Secondly, as noted above, the claims do not limit the 5’ nuclease as “functional or active at about 55°C or higher”. The specific temperature recitations provide examples of preferred limitations or embodiments. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). For these reasons and the reasons already made of record, the rejections are maintained.

Double Patenting

15. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or

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improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

16. Claims 101, 104-106, 111-120 and 122-125 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of copending Application No. 11/031,487. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are coextensive in scope. The claims of the instant application are drawn to a set of reagents comprising a thermostable 5' nuclease lacking synthetic activity, a first oligonucleotide comprising a charged adduct and a portion completely complementary to a target nucleic acid and a second oligonucleotide comprising a 3' portion and a 5' portion wherein the 5' portion is completely complementary to a second region of the target downstream of and contiguous to the first region of the target. Claims 1-7 of the '487 application are drawn to a kit comprising an invasive detection cleavage assay which comprises a first oligonucleotide comprising a 5' portion and a 3' portion which hybridizes to the 5' UTR of HCV (target) and a second oligonucleotide which comprises a 5' portion and a 3' portion wherein the 5' portion hybridizes to the HCV 5' UTR and its 3' portion does not. As defined by the specification of the '487 application, the 2nd oligonucleotide hybridizes to the target downstream of the first oligonucleotide, and a kit comprising "an invasive cleavage detection assay" encompasses a thermostable 5' nuclease (eg: FEN-1), wherein either the 1st or

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2nd oligonucleotide is attached to a solid support, a buffer solution, a third oligonucleotide complementary to a third region of the target upstream of the first region, a charged label which is detectable, including a linker, a detectable molecule, an peptide, an amino modified base and an uncleavable region. Accordingly, the claims of the '487 application and the claims of the instant application are coextensive in scope and not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

17. Claim 121 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-7 of copending Application No. 11/031,487 in view of Corey. The claims of the instant application are drawn to a set of reagents comprising a thermostable 5' nuclease lacking synthetic activity, a first oligonucleotide comprising a charged adduct and a portion completely complementary to a target nucleic acid and a second oligonucleotide comprising a 3' portion and a 5' portion wherein the 5' portion is completely complementary to a second region of the target downstream of and contiguous to the first region of the target. Claims 1-7 of the '487 application are drawn to a kit comprising an invasive detection cleavage assay which comprises a first oligonucleotide comprising a 5' portion and a 3' portion which hybridizes to the 5' UTR of HCV (target) and a second oligonucleotide which comprises a 5' portion and a 3' portion wherein the 5' portion hybridizes to the HCV 5' UTR and it's 3' portion does not. As defined by the specification of the '487 application, the 2nd oligonucleotide hybridizes to the target downstream of the first oligonucleotide, and a kit comprising "an invasive cleavage detection assay" encompasses a

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thermostable 5' nuclease (eg: FEN-1), wherein either the 1st or 2nd oligonucleotide is attached to a solid support, a buffer solution, a third oligonucleotide complementary to a third region of the target upstream of the first region, a charged label which is detectable, including a linker, a detectable molecule, an peptide, an amino modified base and an uncleavable region. Although the claims of the '487 application do not teach a charged peptide which is lysine, arginine, aspartate, or glutamate, Corey teaches peptide-nucleotide adducts comprising lysine. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include the use of lysine in the kit of the '487 application because Corey teaches the use of lysine in peptide-nucleotide adducts, as taught by the claims of the '487 application.

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

18. The response at pages 15-16 traverses the rejections based on obviousness type double patenting with the '487 application. In both rejections over the '487 application, the response asserts that the claims are not coextensive in scope because the claims of the instant application are directed to sets of reagents that are not limited to any particular target nucleic acid or organism while the claims of the '487 application are substantially different in that each of claims 1-7 is limited to a single nucleotide polymorphism. This argument has been thoroughly reviewed but was found unpersuasive as the claims of the '487 application represent a species of the broadly claimed genus of the instant application. The courts have stated that a genus is obvious in view of the teachings of a species. See Slayter, 276 F.2d 408, 411, 125 USPQ 345,

347 (CCPA 1960); and *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614 (Fed. Cir. 1989). For these reasons and the reasons already made of record, the rejections are maintained.

19. Claims 101, 104-106, 111-120, and 122-125 provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 and 24-29 of copending Application No. 10/754,408. Although the conflicting claims are not identical, they are not patentably distinct from each other because they are coextensive in scope. The claims of the instant application are drawn to a set of reagents comprising a thermostable 5' nuclease lacking synthetic activity, a first oligonucleotide comprising a charged adduct and a portion completely complementary to a target nucleic acid and a second oligonucleotide comprising a 3' portion and a 5' portion wherein the 5' portion is completely complementary to a second region of the target downstream of and contiguous to the first region of the target. Claims 1-13 and 24-29 of the '408 application are drawn to a kit comprising oligonucleotides for a non-amplified oligonucleotide detection assay which comprises a first oligonucleotide comprising a 5' portion and a 3' portion which hybridizes to the a target containing a connexin 26 allele and a second oligonucleotide which comprises a 5' portion and a 3' portion wherein the 5' portion hybridizes to the target containing the connexin 26 allele and its 3' portion does not. As defined by the specification of the '408 application, the 2nd oligonucleotide hybridizes to the target downstream of the first oligonucleotide, a non-amplified oligonucleotide detection assay comprises a thermostable 5' nuclease (eg: FEN-1), wherein either the 1st or 2nd oligonucleotide is attached to a solid support, a buffer solution, a third oligonucleotide complementary to a third region of the target upstream of the first region, a charged label which is detectable, including a

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linker, a detectable molecule, an peptide, an amino modified base and an uncleavable region.

Accordingly, the claims of the '408 application and the claims of the instant application are coextensive in scope and not patentably distinct from each other.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

20. Claim 121 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-13 and 24-29 of copending Application No. 10/754,408 in view of Corey. The claims of the instant application are drawn to a set of reagents comprising a thermostable 5' nuclease lacking synthetic activity, a first oligonucleotide comprising a charged adduct and a portion completely complementary to a target nucleic acid and a second oligonucleotide comprising a 3' portion and a 5' portion wherein the 5' portion is completely complementary to a second region of the target downstream of and contiguous to the first region of the target. Claims 1-13 and 24-29 of the '408 application are drawn to a kit comprising oligonucleotides for a non-amplified oligonucleotide detection assay which comprises a first oligonucleotide comprising a 5' portion and a 3' portion which hybridizes to the a target containing a connexin 26 allele and a second oligonucleotide which comprises a 5' portion and a 3' portion wherein the 5' portion hybridizes to the target containing the connexin 26 allele and it's 3' portion does not. As defined by the specification of the '408 application, the 2nd oligonucleotide hybridizes to the target downstream of the first oligonucleotide, a non-amplified oligonucleotide detection assay comprises a thermostable 5' nuclease (eg: FEN-1), wherein either the 1st or 2nd oligonucleotide is attached to a solid support,

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a buffer solution, a third oligonucleotide complementary to a third region of the target upstream of the first region, a charged label which is detectable, including a linker, a detectable molecule, an peptide, an amino modified base and an uncleavable region. Although the claims of the '408 application do not teach a charged peptide which is lysine, arginine, aspartate, or glutamate, Corey teaches peptide-nucleotide adducts comprising lysine. Therefore, it would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to include the use of lysine in the kit of the '408 application because Corey teaches the use of lysine in peptide-nucleotide adducts, as taught by the claims of the '408 application

This is a provisional obviousness-type double patenting rejection.

Response to Arguments

21. At pages 16-18, the response traverses the rejections based on obviousness type double patenting with the '408 application. In both rejections over the '408 application, the response asserts that the claims are not coextensive in scope because the claims of the instant application are directed to sets of reagents that are not limited to any particular target nucleic acid or organism while the claims of the '408 application are substantially different scope in that each of claims 1-13 and 24-29 is configured for detection of a Connexin 26 allele. This argument has been thoroughly reviewed but was found unpersuasive as the claims of the '408 application directed to detecting a specific allele represent a species of the broadly claimed genus of the instant application where the claims are not limited to any particular target. The courts have stated that a genus is obvious in view of the teachings of a species. See *Slayter*, 276 F.2d 408, 411, 125 USPQ 345, 347 (CCPA 1960); and *In re Gosteli*, 872 F.2d 1008, 10 USPQ2d 1614

(Fed. Cir. 1989). The response also asserts that the claims of the '408 application are not limited to the use of the sets of reagents claimed in the present assay. This argument has been thoroughly reviewed but was found unpersuasive as the instant claims are drawn to a set of reagents and are not limited to any particular assay. Further, as noted in the response, one of the assays the claims of the '408 application are selected for are invasive cleavage assays. Accordingly, the claims are coextensive in scope. For these reasons and the reasons already made of record, the rejections are maintained.

Conclusion

22. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

23. No claims are allowable over the cited prior art.

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24. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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Jehanne Sitton
Primary Examiner
Art Unit 1634

5/18/06